PoCoG
Psycho-oncology Co-operative Research Group

Study Closeout

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Study Closeout SOP

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Foreword

The Psycho-Oncology Cooperative Research Group (PoCoG) has developed a program of quality assurance for Psycho-Oncology Research. PoCoG's Quality System requires documentation of both management and procedural activities. This study closeout guidance document provides a standard working tool for the closure of a research study.

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Overview

Study Closeout relates to the closure of a study at participating sites once all subjects have completed the study and all data queries have been resolved.

Closeout is defined as the act of ensuring that all research study related activities are appropriately reconciled, recorded and reported at the end of a trial in accordance with the protocol, SOPs, GCP and the applicable regulatory requirements.

Closeout is an integral part of the QC of a study to ensure that all necessary documents are in place should it be necessary for the study information to be retrieved or inspected in the future.

The study closeout should mean that it is ready for an audit or inspection.

Purpose

The purpose of this SOP is to describe the recommended processes to close/ complete a research study. These processes include:

- Data verification and collection of all remaining completed case report forms (CRFs)
- Inspecting site-specific and centralised files for completeness
- Reviewing the records of intervention distribution, where relevant, including accountability records, inventory and reconciliation. This also includes the return or destruction of materials.
- Discussion of issues and next steps with study personnel. This may include the requirement for follow-up and data retention.

Scope

This SOP outlines the processes to be followed at the end of study data collection or follow-up, by the co-ordinating centre and the recruitment sites.

Guiding Principles

Research studies should be conducted in accordance with applicable legislation and regulatory standards. Thus, this document has been guided by the following resources:

- International Conference on Harmonisation documentation on Good Clinical Practice (ICH-GCP, http://www.ich.org/home.html) and the Therapeutic Goods Administration (TGA) annotated version (http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm).
- the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (henceforth referred to as the 'national statement', http://www.nhmrc.gov.au/publications/synopses/e35syn.htm),
- The Australian Code for the Responsible Conduct of Research (http://www.nhmrc.gov.au/publications/synopses/r39syn.htm),
- Therapeutic Goods Administration's Australian Clinical Trial Handbook (http://www.tga.gov.au/industry/clinical-trials-handbook.htm), and
- Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/index.html).

Definitions and Abbreviations

Adverse Events (AE)	Any untoward occurrence in a study participant. An AE can therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with participation in the study.
Case report form (CRF)	A paper or electronic questionnaire specifically used in clinical research. The CRF is the tool used to collect data. All data on each patient participating in a study are held and/or documented in the CRF, including adverse events.
Chief Investigator (CI)	A Chief Investigator (CI) is involved in the study design, grant applications, research protocol development and is a member of the *Study Management Committee*.
Coordinating centre	The site which the study is coordinated, usually the site where the Principal Investigator is based and where funding is administered.
Data Management (DM)	The development, implementation and supervision of policies relating to the management of study data. This includes mechanisms to protect the data.
Data Management Plan (DMP)	The plan that defines details of policy and implementation of the management of data.
Data queries	A question that is raised by data that is either inconsistent or unclear.
Notes-to-file	These are the notes written in the study files that record a problem that has been identified and describes a procedural change instituted to prevent a recurrence of this problem. It should be signed by the site investigator. This may include incidents that occur at the site, instructions from the coordinating site, problems experienced, and any other matter which is important to understand what has happened in the study. It may also be used to explain unusual data.
Principal Investigator (PI)	The investigator responsible for the co-ordination of Chief Investigators and Site Investigators in a multicentre study. Often the Principal Investigator is also Chief Investigator A (CIA) on grant and ethics applications and will lead the *Study Management Committee*. Also: Coordinating Investigator.
Research Assistant (RA)	A person who assists with conducting the study.
Research Operations Team	The research operations team (distinct from Study Management Committee) are responsible for the general research issues, including safety reporting, ethical considerations, publication policy etc.
Serious Adverse Event (SAE)	Any event that suggests a significant hazard, contraindication, side effect, or precaution, that may jeopardize the participant, whether or not it is considered to be associated with the study, is a SAE.
Standard Operating Procedures (SOPs)	Detailed written instructions designed to achieve uniformity of the performance of a specific function.
Study Management Committee (SMC)	A committee composed of the PI and CIs who manage the study. The SMC usually also includes a statistician, project manager/ study coordinator, representatives of the various disciplines involved in the trial, and consumer

	representatives. Also known as the Trial Management Committee (TMC).
Study-related materials	For the context of this document “study-related materials” include study packages, intervention, and/or investigational product.

Qualifications and Responsibilities

This SOP applies to those members of the Study Management Committee and Research Operations Team involved in study closeout, including the following (as applicable):

- Principal Investigator
- Chief Investigators
- Site Investigators
- Study coordinator
- Research Assistants

1. Procedure(s)

In a multicentre study, closeout occurs in two ways - firstly, at the individual sites (site closeout) and then at the coordinating centre (study closeout). These two processes may occur at different times. For example, site closeout may occur when recruitment ceases, if the site is not involved in the follow-up of participants, several months ahead of study closeout. Formal study closeout occurs after the last participant has completed their final follow-up and the associated case report forms (CRFs) are checked for completeness and submitted. Both closeout procedures will be initiated by the study coordinator. These processes are described separately below, and have been described primarily for the study coordinator.

Please note: For the purposes of this SOP “study-related materials” include study packages, intervention, and/or investigational products.

A) SITE CLOSEOUT

Step	Coordinating centre tasks	Site tasks
1.1. Notification of site closeout	Notify individual sites to arrange a meeting with a site staff member who will assist with the site closeout procedure.	Allocate a staff member to assist with the site closeout procedure.
1.2. Review of study files for completeness	**Check that all documentation has been received** This may include: • Communicate with appropriate site staff for a final inventory of study-related materials. • Checking that all documentation (e.g. CRFs, consents) has been received, entered and filed. • Ensuring that consent forms are signed and dated. • Collecting documentation of protocol violations and deviations, protocol amendments, HREC approvals, other approvals, etc. • Checking that reports of SAEs and AEs have been brought to the attention of the HREC and addressed. • Conducting an inventory of unused study-related materials (e.g. information booklets, recruitment packages, etc).	**Check that all documentation has been sent** This may include: • Communicate with coordinating staff about a final inventory of study-related materials. • Confirming the quantity of unused study-related materials at the site • Ensuring all documentation (e.g. CRFs, consents) has been sent to the coordinating centre (originals or copies as per protocol). • Collating documentation of protocol violations and deviations, protocol amendments, HREC approvals, other approvals, etc. and sent to the coordinating centre. • Ensuring that reports of SAEs and AEs have been brought to the attention of the HREC and addressed. • Arranging a visit to the site, as appropriate, and ensuring that appropriate/ relevant records will be available for review
	Completion of all outstanding action items This may include: • Ensuring that outstanding ethics notifications for SAEs and AEs have been submitted. • Following-up on missing consent forms • Determine if any site visits are required. A site visit may be required to close the study, to collect remaining study documents, to check data has been entered correctly, or to review relevant medical records etc. If a visit is required	**Completion of all outstanding action items** This may include: • Completing ethics notifications for SAEs and AEs. • Contacting relevant people for missing consent forms

Step	Coordinating centre tasks	Site tasks
	consider: – The purpose of the visit. – Which departments need visiting – The duration of the visit	
	Review investigator files for completeness This includes resolving discrepancies in investigator files and recording notes-to-file (records of problems and/ or instituted procedural changes) regarding data recorded on CRFs. This may include checking for missing CVs and signature logs.	
1.3. Verify all data recorded	**Ensure all data queries* are resolved.** *Data queries are the items that have been returned from the database as a query. For example, if the date of diagnosis in the database is after the date that treatment commences, this should raise a query and the dates should be checked to attempt to resolve this query.	
	Complete/ collect any outstanding Case Report Forms (CRFs) including notes-to-file. This includes ensuring that any corrections, additions or deletions are made, dates, explained, initialed by the authorized persons, and compared against source documents (if necessary). Notes-to-file are written in the study file and record a problem that has been identified and/ or describes a procedural change instituted to prevent a recurrence of this problem. It should be signed by the site investigator. This may include incidents that occur at the site, instructions from the coordinating site, problems experienced, and any other matters which are crucial to understand what has happened in the study. It may also be used to explain unusual data, for example, if a participant is reported at 2m tall and weigh 68kg this might raise a query in the database, so a note-to-file may need to be added to indicate that this is accurate measurement and the man is unusually tall.	
	Check CRFs against source documents.	

Step	Coordinating centre tasks	Site tasks
	Some studies will check that the data collected in the CRFs correspond to the source documents as a quality control mechanism. Refer to the data management plan for specifics for checking the CRFs against source documents.	
1.4. Management of study-related materials	**Ensure accountability of study-related materials** This may include: • In the case of an intervention, reconcile the numbers of the intervention that have been distributed/ that remain at the sites or are with the source of the intervention, where applicable. • Collating and filing copies of packing slips and shipment receipts	**Ensure accountability of study-related materials** This may include: • Collating and filing copies of packing slips and shipment receipts • Complete an audit of remaining materials and send this to the coordinating site (accountability log)
		Ensure notes-to-file exist for any violations/ deviations associated with the handling and use of the study-related materials.
	Arrange for the return of ALL study materials that are required to be retained, as per regulatory requirements. The coordinating site is responsible for notifying the sites about the types of documents that need to be returned. Sites may choose to retain a copy of study materials, details on the type of data and permissions for use are to be outlined in the Clinical Trials Agreement.	**Arrange for the return of ALL study materials that are required to be retained, as per regulatory requirements.**
	Arrange for return of other study-related materials and arrange for the destruction study materials. This may include: • Inform sites which documents are to be destroyed, when, and in what manner. • File copies of all product shipping receipts and accountability records for the returned materials or copies of the destruction log.	**Arrange for return of other study-related materials or provide documentation of destruction.** This may include: • Providing a log of study-related materials which are destroyed.
1.5. Ensure sponsor/	This may include: • Providing plans for publications	This may include: • Setting up requests for invoices and anticipating timing

Step	Coordinating centre tasks	Site tasks
collaborative agreements are finalised	• Providing feedback to sites regarding performance. • Plans for inspections or audits • Preparation of final reports.	to received outstanding payments. • Preparation of final reports.
1.6. Study site closure report	It is recommended that a study site closure report is completed. This should include the following details: • The number of participants enrolled at the site • The number of participants who have completed the study • The number of participants who have been lost to follow-up, including the reasons for this. • A list of SAEs/ AEs • Information about the final ethics report (i.e. date submitted). Please refer to SOP_10.3.1 for a template site closure report.	Confirmation that details outlined in the study site closure form are correct.
1.7. Updating study status – this step is only relevant if the coordinating site will be continuing with the study long after sites are closed.	**Clinical trials registers** If recruitment has ceased at all sites (but the study is still undergoing follow-up), the coordinating centre should notify the clinical trials register of the change in study status. Refer to the instructions of the clinical trials register where trial has been registered (e.g. the Australian and New Zealand Clinical Trials Register, ANZCTR) for guidance.	**Ethics committees** Refer to individual ethic committee requirements for updates and amendments. If recruitment has ceased at all sites (but the study is still undergoing follow-up), it is likely that the HREC should be notified of the change in study status at this site.

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B) STUDY CLOSEOUT

The process described below for study closeout can only be completed at the coordinating site after all the individual sites have undergone site closeout (as described above).

1.1. Review of study files for completeness

Confirm that all documentation has been received and verified.

1.2. Management of study-related materials

Confirm accountability of all study materials that have been either returned or destroyed at the sites. Also determine the documents of value at the coordinating centre that require retention.

1.3. Ensure sponsor/ collaborative agreements are finalised

Check that all sites have been paid according to previous agreement and that feedback had been provided.

1.4. Review site closure reports for completeness

This is a QA measure to ensure that all the relevant paper work has been completed.

1.5. Inform ethics committees about study closure

Refer to individual ethics committee requirements for study closure – this will often include the completion of a final report

1.6. Inform the clinical trials register that the study is closed.

Refer to the instructions of the clinical trials register where trial has been registered for the process.

1.7. Inform PoCoG of the change in study status.

Where possible, PoCoG endorsed studies should notify PoCoG of study closure during the next round of reporting.

1.8. Send summary to sites with key findings and conclusions.

It is recommended that a summary of key findings and conclusions drawn from the study is sent to the stakeholders, including the study investigators and representatives at sites. This may include participants if they have been offered this option in the consenting process.

1.9. Retention, archiving and destruction of records.

Refer to the study's data management plan (SOP_4.0.0) for details of record retention and archiving of data. Issues to consider include:

- Abiding by the institutional/ organisational requirements for storage of data.
- Ensuring that electronic data will be maintained in compliance with regulatory standards.
- Determining when and if hard copies will be printed out for storage.
- Packing up and labelling of the documents to be archived.
- Allocating responsibility of the archived data (this will usually be the Principal Investigator).
- Arranging the transfer/ storage of documents to archives (These include: participant files, study protocol, signed consent forms, CRFs, questionnaires, ethics correspondence and approvals, other regulatory documentation, and other documents pertaining to the conduct of the study).
- Confirming that this data has not been archived previously (if yes, when and by whom).
- Arranging the destruction of unneeded documents and data.

2. Records management

Documentation of the study closure process is important. It is the responsibility of the study coordinating centre and the principal investigator to ensure that all the approvals, notifications, and documentation required as part of study closure is signed and completed. The data management plan will be useful in successfully completing this process, and archived documents are to be listed on the study specific archives register (SOP_4.3.7). SOP_10.3.2 is a checklist that staff can tick off with the completion of closeout procedures at a site and SOP_10.3.3 is a checklist for study closure.

3. Quality Assurance (QA) - templates, forms and checklists

3.1. Site Closure Report Template

This template (SOP_10.3.1) can be used to document the recruitment at each site and whether ethics final reports have been submitted. This form has been designed to be completed by the co-ordinating site via a discussion (either at a site meeting or over the phone)for each recruitment site.

3.2. Site Closeout Checklist

A checklist (SOP_10.3.2) that outlines the key steps undertaken upon closure of a study at a site. This checklist has been designed to be completed by the co-ordinating site for co-ordinating the closure at each recruitment site. It is also recommended that the sites be sent this checklist as notification of items that need to be completed and will be discussed for the site closure report.

3.3. Study Closeout Checklist

A checklist (SOP_10.3.3) that outlines the key steps undertaken upon closure of a study. This checklist has been designed to be completed by the co-ordinating site for complete study closure.

3.4. Recruitment Site Report Form

This form (SOP_10.3.4) can be used to document the closeout process at recruitment sites. This is to be completed by the co-ordinating site via a discussion (either at a site meeting or over the phone) for each recruitment site. Please note this form is for sites that ONLY recruit but do not obtain informed consent or have any other involvement in the study